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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,771	03/22/2004	Vivian Y.H. Hook	066817-0024	2420

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EXAMINER

HEARD, THOMAS SWEENEY

ART UNIT	PAPER NUMBER
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1654

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03/31/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/806,771	Applicant(s) HOOK, VIVIAN Y.H.	
	Examiner THOMAS S. HEARD	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 2 and 5-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3 and 4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>01/28/2008</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1, Claims 1, and 3-5 in the reply filed on 1/28/2008 is acknowledged.

Claims 2, 5-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 1/28/2008. Applicants have made the remark that they traverse but have not provided a reason for the traverse. Therefore, the election of Group and Species is treated as with traverse. Since Applicants have elected the species, Cathepsin B, Claim 5 is withdrawn from further consideration, as being drawn to non-elected subject matter.

Claims 1, 3, and 4 are hereby examined on the merits.

Claim Objections

Claim 1 is objected to because of the following informalities: Claim 1 depends from a higher numbered claim. Appropriate correction is required.

Nucleotide Sequence and/or Amino Acid Sequence Disclosures

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below. **All sequences disclosed in the application must comply with the requirements of 37 C.F.R. 1.821-1.825, not only those recited in the claims.**

In the drawings submitted 3/22/2004, there are amino acids sequences that do not have proper identifiers. Applicants must have a SEQ ID associated with any amino

Art Unit: 1654

acid sequence of four or more amino acids in length. Applicants should carefully check the specification to assure SEQ ID NOs are associated with all peptide four or more amino acids in length, even though they may not be claimed sequences.

Information Disclosure Statement

A signed and considered IDS accompanies this Office Action. Only US patents and WO documents have been considered because the Applicants have not submitted the Non-Patent literature (NPL) indicated on the IDS summary. Applicants must submit the appropriate NPL for consideration on the next action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 3, it is not understood what an APP substrate is. APP is a substrate for cathepsin B, but Applicants are claiming an APP substrate which is indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

Art Unit: 1654

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining

obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

For the purpose of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. *Joy Technologies Inc. V. Quigg*, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held in accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In *re Hoeschele*, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In *re Clinton*, 188 USPQ 365, 367 (CCPA 1976); In *re Thompson*, 192 USPQ 275, 277 (CCPA 1976).

Claims 1, 3, and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagao et al, "Synthesis of a new class of cathepsin B inhibitors exploiting a unique reaction cascade," *Tetrahedron Letters*, 41 (2000), 2419-2424 and Mackay EA et al "A possible role for cathepsins D, E, and B in the processing of beta-amyloid precursor protein in Alzheimer's disease," *Eur J Biochem*. 1997 Mar 1;244(2):414-25.

The instant claims are drawn to a method of selecting an agent that prevents the cleavage of an APP by the proteolytic action of cathepsin B.

Nagao et al teaches an assay where cathepsin B inhibitors are incubated in the presence of a cathepsin B peptide substrate, Z-L-Phe-L-Arg-MCA, see page 2421 and last paragraph for the assay. Nagao et al does not teach the use of APP as a cathepsin B substrate.

Mackay et al discloses the proteolytic action of cathepsin D, E, and B (Applicant's elected species), on the amyloid precursor protein (APP). Mackay et al teaches the use of MALDI-TOF mass spectroscopy to identify the position of cleavage of cathepsin D, E, and B, see Figure 3 and Figure 5. Mackay et al does not teach the use of an inhibitor of cathepsin D, E, or B in the assay to inhibit the action of cathepsin B.

The difference between what is taught by the prior art and that instantly claimed is that the instant invention claims an assay to screen for inhibitors of cathepsin B toward APP, and the prior art teaches that there are cathepsin B inhibitor assays already developed but do not use APP as the substrate (Nagao et al) but that APP is a substrate of cathepsin B (Mackay et al).

It would have been obvious to one of ordinary skill in the art to modify the assay taught by Nagao et al to substitute the B peptide substrate, Z-L-Phe-L-Arg-MCA, with that of APP. One would have been motivated to do this because Mackay teaches that APP is a substrate for cathepsin B. One would have had a reasonable expectation of success in substituting APP for Z-L-Phe-L-Arg-MCA because cathepsin B can hydrolyze both Z-L-Phe-L-Arg-MCA and APP, and those inhibitors blocked cathepsin B and would also block the hydrolysis of APP. One would be further motivated to continue screening for compounds that inhibit the catalysis of APP because the hydrolytic fragments are known to be involved in the formation of Alzheimer's disease, and that one would be motivated to identify these inhibitors for potential therapeutic use. Conversely, from the combined teaching of the Mackay et al and Nagao et al references, it would have been obvious to modify the Mackay et al teachings to add the inhibitors of Nagao et al,

Art Unit: 1654

as well as any other compound, to determine whether the compound blocked cathepsin B activity and produced full length APP proteins as determined by MALDI-TOF mass spectroscopy. One would have a reasonable expectation of success because of the detailed information revealed from MALDI-TOF mass spectroscopy, which include the position of cleavage by mass if the compound did not inhibit cathepsin B. From the teachings of the references supra, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, and the invention as claimed, is rejected under 35 U.S.C. 103(a).

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Prior art contained in the reference of record can be applied in the next office action.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1654

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thomas S Heard/

Examiner, Art Unit 1654

/Anish Gupta/

Primary Examiner, Art Unit 1654